

REMARKS

Claims 36, 37 and 54-72 were pending in this application. Claim 36 has been amended. Support for this amendment can be found in the specification, for example, on page 2, lines 2-5; page 6, lines 19-24 and in the claims as originally filed. New claim 73 has been added. Therefore, claims 36, 37 and 54-73 are pending with claim 36 being an independent claim.

No new matter has been added.

Rejection Under 35 U.S.C. §112

The Examiner has rejected claim 70 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner has argued that the phrase “heparin-like glycosaminoglycan” is vague and indefinite.

Applicant respectfully traverses this rejection. Applicant maintains that one of ordinary skill in the art would be reasonably apprised of the meaning of this term, as the term is not only defined in the specification (See, e.g., page 12, lines 23-30) but was also known to those of ordinary skill in the art at the time the application was filed. To satisfy the written description requirement for definiteness, it is sufficient to show that one of ordinary skill in the art would understand and be able to interpret the rejected term along with the scope of the claim. Applicant maintains that this is the case.

The instant specification clearly defines the term “heparin-like glycosaminoglycan” as a complex polysaccharide made up of disaccharide repeat units comprising hexosamine and glucuronic/iduronic acid that are linked by α/β 1-4 glycosidic linkages. Further, the defining units may be modified by sulfation and/or acetylation. In addition to the definition provided, the term has been in use, by those of ordinary skill in the art, since as early as 1969, according to a review of the references available in the PubMed database. A search of the PubMed database on September 5, 2006 for “heparin-like glycosaminoglycan” or “HLGAG” resulted in the identification of twenty (20) different journal articles published prior to the priority date of the instant application. Therefore, at least this many articles containing one or both of these terms were published prior to the priority date of this application. A list of the journal articles that were identified is provided for the Examiner’s review.

As heparin-like glycosaminoglycans are defined in the instant specification and demonstrated to have been known to those of ordinary skill in the art prior to the time of the filing of the instant application, Applicant maintains that one of ordinary skill in the art would understand what molecules are encompassed by the term and would, therefore, recognize the scope of rejected claim 70. Accordingly, Applicant respectfully requests the Examiner to withdraw the rejection of claim 70 under 35 U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. §102

The Examiner has rejected claims 36, 37, 54-64 and 66-72 under 35 U.S.C. §102(b) as being allegedly anticipated by van Kuik et al. (Carbohydrate Research, Vol. 235, 1992, pages 53-68).

Applicant respectfully traverses this rejection. However, in the interest of expediting prosecution of this application and without conceding the correctness of the Examiner's rejection, Applicant has amended claim 36. The amendment adds the limitation that the identifier includes a value for a disaccharide of the polysaccharide. Applicant notes that van Kuik et al. do not provide a teaching whereby disaccharides are represented.

Further, Applicant wishes to note for the record that there are limitations of the rejected dependent claims that are also not provided by van Kuik et al. contrary to the Examiner's assertions. First, van Kuik et al. do not provide that the identifiers can be represented as a single digit hexadecimal number. The passage that is referred to by the Examiner shows a numbering scheme of certain portions of a branched oligosaccharide that uses a series of integers (1-8) and integers prime (4'-8'). This is not a hexadecimal numbering scheme whereby a base 16 is used, the first 10 digits of which are 0-9 and the next 6 are A-F. Second, van Kuik et al. do not teach comparing monosaccharides or disaccharides with values representing a property comprising charge. Rather, the brief mention of negative charge of the fractions used to test the method of van Kuik et al. was merely provided as general information about the fractions used and was not a teaching that such a property can be used in a method of comparing monosaccharides or disaccharides. Third, the Examiner alleges that van Kuik et al. teach preparing oligosaccharides with a certain enzyme, which allegedly somehow represents properties comprising the nature and degree of sulfation and acetylation. The teaching referred to on page 57, second paragraph, of

van Kuik et al., however, merely provides how the oligosaccharides used in the van Kuik et al. method were obtained. There is no teaching of these particular properties nor that these properties can be used in the method of van Kuik et al. or the methods of Applicant's claims. Finally, the Examiner alleges that the use of carbohydrate fractions from a pool of horse serum glycoproteins is a teaching of a monosaccharide of a heparin-like glycosaminoglycan. Applicant disagrees. The recitation of horse serum glycoproteins merely indicates that there were glycoproteins in the fractions. However, there is no indication what specific glycoproteins were present, nor that they were heparin-like glycosaminoglycans.

Accordingly, the rejection of claims 36, 37, 54-64 and 66-72 under 35 U.S.C. §102(b) is respectfully requested to be withdrawn.

Rejections Under 35 U.S.C. §103

The Examiner has rejected claim 65 under 35 U.S.C. §103(a) as being unpatentable over van Kuik et al. (Carbohydrate Research, Vol. 235, 1992, pages 53-68) and further in view of van Kuik et al. (Trends in Biotechnology, Vol. 10, 1992, pages 182-185).

Applicant respectfully traverses the rejection. However, in light of the amendment of claim 36 and the inapplicability of van Kuik et al. (Carbohydrate Research, Vol. 235, 1992, pages 53-68) as described above, Applicant maintains that this rejection is now moot.

Accordingly, the rejection of claim 65 under 35 U.S.C. §103(a) is respectfully requested to be withdrawn.

Serial No.: 09/557,997
Conf. No.: 7686

- 9 -

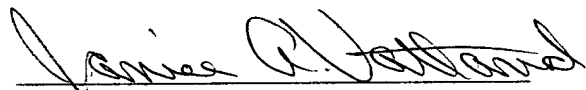
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CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,



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Items 1 - 20 of 31

Page 1

of 2 Next

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Fabrication of chondroitin sulfate-chitosan composite artificial extracellular matrix for stabilization of fibroblast growth factor. J Biomed Mater Res A. 2006 Jan;76(1):1-15. PMID: 16224775 [PubMed - indexed for MEDLINE]

☐ 2: [Naggar EF, Costello CE, Zaia J.](#) [Related Articles, Links](#)



Competing fragmentation processes in tandem mass spectra of heparin-like glycosaminoglycans. J Am Soc Mass Spectrom. 2004 Nov;15(11):1534-44. PMID: 15519220 [PubMed - indexed for MEDLINE]

☐ 3: [Zaia J, Costello CE.](#) [Related Articles, Links](#)



Tandem mass spectrometry of sulfated heparin-like glycosaminoglycan oligosaccharides. Anal Chem. 2003 May 15;75(10):2445-55. PMID: 12918989 [PubMed - indexed for MEDLINE]

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Targeted gene disruption of natural anticoagulant proteins in mice. Int J Hematol. 2002 Aug;76 Suppl 2:36-9. Review. PMID: 12430897 [PubMed - indexed for MEDLINE]

☐ 5: [Kwan CP, Venkataraman G, Shriver Z, Raman R, Liu D, Qi Y, Varticovski L, Sasisekharan R.](#) [Related Articles, Links](#)












Probing fibroblast growth factor dimerization and role of heparin-like glycosaminoglycans in modulating dimerization and signaling. J Biol Chem. 2001 Jun 29;276(26):23421-9. Epub 2001 Apr 5. PMID: 11292822 [PubMed - indexed for MEDLINE]

☐ 6: [Marks RM, Lu H, Sundaresan R, Toida T, Suzuki A, Imanari T, Hernaiz MJ, Linhardt RJ.](#) [Related Articles, Links](#)



Probing the interaction of dengue virus envelope protein with heparin: assessment of glycosaminoglycan-derived inhibitors. J Med Chem. 2001 Jun 21;44(13):2178-87. PMID: 11405655 [PubMed - indexed for MEDLINE]

☐ 7: [Shriver Z, Raman R, Venkataraman G, Drummond K, Turnbull J, Toida T, Linhardt R, Biemann K, Sasisekharan R.](#) [Related Articles, Links](#)

-  Sequencing of 3-O sulfate containing heparin decasaccharides with a partial antithrombin III binding site.
Proc Natl Acad Sci U S A. 2000 Sep 12;97(19):10359-64.
PMID: 10984531 [PubMed - indexed for MEDLINE]
- ☐ **8:** [Ali S, Palmer AC, Banerjee B, Fritchley SJ, Kirby JA.](#) [Related Articles](#), [Links](#)
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J Biol Chem. 2000 Apr 21;275(16):11721-7.
PMID: 10766793 [PubMed - indexed for MEDLINE]
- ☐ **9:** [Venkataraman G, Shriver Z, Raman R, Sasisekharan R.](#) [Related Articles](#), [Links](#)
-  Sequencing complex polysaccharides.
Science. 1999 Oct 15;286(5439):537-42.
PMID: 10521350 [PubMed - indexed for MEDLINE]
- ☐ **10:** [Padera R, Venkataraman G, Berry D, Godavarti R, Sasisekharan R.](#) [Related Articles](#), [Links](#)
-  FGF-2/fibroblast growth factor receptor/heparin-like glycosaminoglycan interactions: a compensation model for FGF-2 signaling.
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- ☐ **11:** [Feldman SA, Hendry RM, Beeler JA.](#) [Related Articles](#), [Links](#)
-  Identification of a linear heparin binding domain for human respiratory syncytial virus attachment glycoprotein G.
J Virol. 1999 Aug;73(8):6610-7.
PMID: 10400758 [PubMed - indexed for MEDLINE]
- ☐ **12:** [Venkataraman G, Raman R, Sasisekharan V, Sasisekharan R.](#) [Related Articles](#), [Links](#)
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Proc Natl Acad Sci U S A. 1999 Mar 30;96(7):3658-63.
PMID: 10097093 [PubMed - indexed for MEDLINE]
- ☐ **13:** [Venkataraman G, Shriver Z, Davis JC, Sasisekharan R.](#) [Related Articles](#), [Links](#)
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- ☐ **14:** [Liu D, Shriver Z, Godavarti R, Venkataraman G, Sasisekharan R.](#) [Related Articles](#), [Links](#)
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J Biol Chem. 1999 Feb 12;274(7):4089-95.
PMID: 9933602 [PubMed - indexed for MEDLINE]
- ☐ **15:** [Natke B, Venkataraman G, Nugent MA, Sasisekharan R.](#) [Related Articles](#), [Links](#)
-  Heparinase treatment of bovine smooth muscle cells inhibits fibroblast growth factor-2 binding to fibroblast growth factor receptor but not FGF-2 mediated cellular proliferation.
Angiogenesis. 1999;3(3):249-57.
PMID: 14517424 [PubMed]
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Syndecans, heparan sulfate proteoglycans, maintain the proteolytic balance of acute wound fluids. *J Biol Chem.* 1998 May 8;273(19):11563-9. PMID: 9565572 [PubMed - indexed for MEDLINE]

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Heparinase II from *Flavobacterium heparinum*. Role of histidine residues in enzymatic activity as probed by chemical modification and site-directed mutagenesis. *J Biol Chem.* 1998 Apr 24;273(17):10160-7. PMID: 9553064 [PubMed - indexed for MEDLINE]

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On the regulation of fibroblast growth factor activity by heparin-like glycosaminoglycans. *Angiogenesis.* 1997;1(1):45-54. PMID: 14517393 [PubMed - as supplied by publisher]

Items 1 - 20 of 31

Page 1

of 2 Next

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Items 21 - 31 of 31

Previous

Page

2

of 2

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An environmentally regulated receptor for diamine oxidase modulates human endothelial cell/fibroblast histamine degradative uptake.

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PMID: 8195119 [PubMed - indexed for MEDLINE]

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[Heparan sulfate proteoglycan of endothelial cells: homocysteine suppresses anticoagulant active heparan sulfate in cultured endothelial cells]

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- ☐ **23:** Visentin GP, Ford SE, Scott JP, Aster RH. [Related Articles](#), [Links](#)



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Homocysteine, a thrombogenic agent, suppresses anticoagulant heparan sulfate expression in cultured porcine aortic endothelial cells.

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Heparin-like glycosaminoglycan is a receptor for antithrombin III-dependent but not for thrombin-dependent prostacyclin production in human endothelial cells.

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D-[3H]glucosamine labelling of epidermal and dermal glycosaminoglycans in cultured human skin.
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Fibroblast growth factors are present in the extracellular matrix produced by endothelial cells in vitro: implications for a role of heparinase-like enzymes in the neovascular response.
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☐ **30:** [Radhakrishnamurthy B, Sharma C, Bhandaru RR, Berenson GS, Stanzani L, Mastacchi R.](#)

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Studies of chemical and biologic properties of a fraction of sulodexide, a heparin-like glycosaminoglycan.
Atherosclerosis. 1986 May;60(2):141-9.
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☐ **31:** [Olivecrona T, Lindahl U.](#)

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Items 21 - 31 of 31

[Previous](#)

Page 2

of 2

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